Applicant: Alan Wellington Faull et al.

Serial No.: To Be Assigned

Filed : Herewith Page : 3 of 11

Attorney's Docket No.: 06275-461US1 / 100929-1P US

10/542326

JC17 Rec'd PCINTO 13 JUL 2005

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Original) A compound of formula (I)

$$\begin{array}{c|c} & & & & \\ & & & & \\ & & & & \\$$

wherein

R¹ represents H or CH₃;

 R^2 represents hydrogen, halogen, cyano, C1 to 2 alkyl, trifluoromethyl or C1 to 2 alkoxy; R^3 and R^4 independently represent H or CH_3 ;

or the group CR³R⁴ together represents a C3 to 6 cycloalkyl ring;

A represents a six-membered aromatic ring optionally incorporating one or two nitrogen atoms; and the group -CR³R⁴-X-R⁵ is bonded to ring A in the 4-position relative to the thiophene ring;

X represents NR⁶;

Applicant: Alan Wellington Faull et al. Attorney's Docket No.: 06275-461US1 / 100929-1P US

Serial No.: To Be Assigned

Filed : Herewith
Page : 4 of 11

R⁵ represents H, C1 to 6 alkyl, C2 to 6 alkenyl or C3 to 6 cycloalkyl; said cycloalkyl group optionally incorporating one heteroatom selected from O, S(O)_n or NR⁷; said alkyl group being optionally further substituted by one or more groups selected independently from CN, OH, C1 to 4 alkoxy, F, a C5 to 10 monocyclic or bicyclic aromatic ring system optionally incorporating one or two heteroatoms independently selected from O, S and N, and said ring system being optionally further substituted by one or more substituents selected independently from halogen, C1 to 2 alkyl, C1 to 2 alkoxy or CF₃; or said alkyl being optionally further substituted by a C5 to 6 cycloalkyl ring that optionally incorporates a heteroatom selected from O, S(O)_m or NR⁸ and/or a carbonyl group and is optionally further substituted by OH;

R⁶ represents H or C1 to 6 alkyl; said alkyl group being optionally further substituted by CN, OH, C1 to 4 alkoxy or one or more fluoro atoms;

n and m independently represent an integer 0, 1 or 2; R⁷ and R⁸ independently represent H or C1 to 2 alkyl; and pharmaceutically acceptable salts thereof.

- 2. (Original) A compound of formula (I), according to Claim 1, wherein R¹ represents H.
- 3. (Currently amended) A compound of formula (I), according to Claim 1 or Claim 2, in which A represents optionally substituted phenyl.
- 4. (Currently amended) A compound of formula (I), according to any one of Claims $\frac{1 \text{ to } 3}{2 \text{ Claim } 1}$, in which R^3 and R^4 each represent H.
- 5. (Currently amended) A process for the preparation of a compound of formula (I), according to any one of Claims 1 to 4 Claim 1, which comprises:
 - (a) reaction of a compound of formula (II):

Attorney's Docket No.: 06275-461US1 / 100929-1P US

1

Applicant: Alan Wellington Faull et al.

Serial No.: To Be Assigned

Filed: Herewith Page: 5 of 11

$$\begin{array}{c|c} & & & & \\ & & & & \\ R^1 & & & & \\ & & & & \\ NH_2 & & & \\ & & & \\ & & & \\ CR^3R^4 & & \\ & & & \\ X & & & \\ & & & \\ R^5 & & & \\ \end{array}$$

wherein A, R¹, R², R³, R⁴, R⁵ and X are as defined in Claim 1 with an isocyanate; or
(b) reaction of <u>a</u> compound of formula (III)

$$\begin{array}{c|c} R^2 & \text{Metal} \\ \hline A & \\ \hline CR^3R^4 & \\ \hline X & \\ R^5 & \\ \end{array}$$

wherein A, R^2 , R^3 , R^4 , R^5 and X are as defined in Claim 1, with a compound of formula (IV)

wherein R¹ is as defined in Claim 1 and LG represents a leaving group; or

Applicant: Alan Wellington Faull et al.

Serial No.: To Be Assigned

Filed: Herewith Page: 6 of 11

(c) reaction of <u>a</u> compound of formula (V)

$$R^2$$
 A
 CR^3R^4
 V
 R^5
 C

wherein A, R^2 , R^3 , R^4 , R^5 and X are as defined in Claim 1 and LG represents a leaving group,

with a compound of formula (VI)

wherein R¹ is as defined in Claim 1; or

(d) reaction of <u>a</u> compound of formula (VII)

Attorney's Docket No.: 06275-461US1 / 100929-1P US

Applicant: Alan Wellington Faull et al.

Serial No.: To Be Assigned Filed: Herewith

Filed : Herewith Page : 7 of 11

$$R^{2} \longrightarrow NH_{2}$$

$$R^{2} \longrightarrow NH_{2}$$

$$CR^{3}R^{4} \longrightarrow LG$$

$$(VII)$$

wherein A, R^1 , R^2 , R^3 and R^4 are as defined in Claim 1, and LG represents a leaving group,

with an amine of formula R⁵R⁶NH, wherein R⁵ and R⁶ are as defined in Claim 1; or (e) reaction of <u>a</u> compound of formula (VIII)

wherein A, R¹, R² and R³ are as defined in Claim 1,

with an amine of formula R⁵R⁶NH wherein R⁵ and R⁶ are as defined in Claim 1, under reductive amination conditions; or

(f) reaction of a compound of formula (IX)

Attorney's Docket No.: 06275-461US1 / 100929-1P US

Applicant: Alan Wellington Faull et al.

Serial No.: To Be Assigned

Filed: Herewith Page: 8 of 11

wherein R¹, R², R³, R⁴, R⁵ and A are as defined in Claim 1, with an aldehyde or ketone under reductive amination conditions:

and where necessary converting the resultant compound of formula (I), or another salt thereof, into a pharmaceutically acceptable salt thereof; or converting the resultant compound of formula (I) into a further compound of formula (I); and where desired converting the resultant compound of formula (I) into an optical isomer thereof.

- 6. (Currently amended) A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1 to 4 Claim 1 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.
- 7. (Currently amended) A pharmaceutical composition adapted for administration by inhalation or insufflation[[.]] comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1 to 6 Claim 1 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.
- 8. (Currently amended) A process for the preparation of a pharmaceutical composition as claimed in Claim 6 which comprises mixing a compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1 to 4 Claim 1 with a pharmaceutically acceptable adjuvant, diluent or carrier.

Applicant: Alan Wellington Faull et al. Attorney's Docket No.: 06275-461US1 / 100929-1P US

Serial No.: To Be Assigned

Filed: Herewith
Page: 9 of 11

- 9. (Cancelled)
- 10. (Cancelled)
- 11. (Currently amended) A method for the treatment or prophylaxis of inflammatory disease, comprising administering to a person suffering from or at risk of said disease a therapeutically effective amount [[Use]] of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in Claim 1 any one of claims 1 to 4 in the manufacture of a medicament for use in the treatment or prophylaxis of inflammatory disease.
- 12. (Currently amended) The [[use]] <u>method</u> as claimed in Claim 11 wherein the disease is rheumatoid arthritis.
- 13. (Currently amended) The [[use]] method as claimed in Claim 11 wherein the disease is chronic obstructive pulmonary disease.
 - 14. (Cancelled)
- 15. (Currently amended) A method of treating, or reducing the risk of, diseases a disease or conditions condition in which inhibition of IKK-2 activity is beneficial which comprises administering to a person suffering from or at risk of said disease or condition a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, as claimed in any one of claims 1 to 4 Claim 1.
- 16. (New) A compound of formula (I), according to Claim 2, in which A represents optionally substituted phenyl.

Applicant: Alan Wellington Faull et al. Attorney's Docket No.: 06275-461US1 / 100929-1P US

Serial No.: To Be Assigned

Filed: Herewith Page: 10 of 11

17. (New) A compound of formula (I), according to Claim 2, in which R³ and R⁴ each represent H.

- 18. (New) A compound of formula (I), according to Claim 3, in which R³ and R⁴ each represent H.
- 19. (New) A compound of formula (I), according to Claim 16, in which R³ and R⁴ each represent H.
 - 20. (New) The method as claimed in Claim 15 wherein the disease is cancer.